

CLAIMS

1. A method for screening for a candidate drug to relieve oxidative stress in an endothelial cell comprising:
 - (a) contacting an endothelial cell with DHE;
 - (b) contacting the endothelial cell with a candidate substance;
 - (c) subjecting the endothelial cell to physiologic shear; and
 - (d) comparing the amount of DHE oxidized by the cell with the amount of DHE oxidized by a cell not contacted with the candidate substance.
2. The method of claim 1, wherein the cell is contacted with about 1.0 μM to about 5.0 μM of DHE.
3. The method of claim 1, further comprising exposing the endothelial cell to hydrogen peroxide.
4. The method of claim 3, wherein the cell is exposed to about 30 μM to about 100 μM of hydrogen peroxide.
5. The method of claim 4, wherein the cell is contacted with about 1.0 μM to about 5.0 μM of DHE.
6. The method of claim 1, further comprising contacting the cell with an inhibitor of eNOS, NADPH, endothelial nitric oxide synthase, NADH/NADPH-oxidase, cyclooxygenase, or xanthine oxidase.
7. A method of identifying a target or pathway involved in endothelial cell function comprising:
 - (a) providing an endothelial cell;
 - (b) contacting said endothelial cell with (i) a first substance that acts as an indicator of a first cell function in said endothelial cell and (ii) a modulator of a known enzyme, receptor, transporter, signaling molecule, or transcription factor;
 - (c) subjecting said endothelial cell to physiologic shear; and
 - (d) assessing said first cell function;

wherein a change in said first cell function in the presence of said modulator, as compared to said first cell function in the absence of said modulator, identifies said inhibitor as acting on a target or pathway involved in said first cell function.

8. The method of claim 7, wherein said first cell function is NO production.
9. The method of claim 8, wherein first substance is DHE, and said method further comprises contacting said endothelial cell with H_2O_2 .
10. The method of claim 7, wherein said modulator is an agonist of said first cell function.
11. The method of claim 7, wherein said modulator is an antagonist of said first cell function.
12. The method of claim 7, wherein said modulator acts on an enzyme.
13. The method of claim 12, wherein said modulator is an antagonist of eNOS, NADPH, endothelial nitric oxide synthase, NADH/NADPH-oxidase, cyclooxygenase, or xanthine oxidase.
14. The method of claim 7, wherein said modulator acts on a receptor.
15. The method of claim 9, wherein H_2O_2 is present at about 30 μm to about 100 μm .
16. A method of inhibiting NO production in an endothelial cell comprising contacting said cell with an inhibitor of eNOS, NADPH, endothelial nitric oxide synthase, NADH/NADPH-oxidase, cyclooxygenase, xanthine oxidase.
17. The method of claim 16, wherein said endothelial cell is located in a living organism.
18. The method of claim 17, wherein said living organism is suffering from a disease state.
19. The method of claim 18, wherein said disease state is diabetes or cardiovascular disease.
20. The method of claim 16, wherein said inhibitor is L-NAME or L-NNA.

21. The method of claim 17, wherein said living organism is a human.